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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,934	08/25/2006	Masayuki Tsuchiya	14875-151US1 C1-A0305P-US	1453

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EXAMINER	
GUSSOW, ANNE	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
03/16/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/550,934	TSUCHIYA ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-59* is/are pending in the application.

4a) Of the above claim(s) *32-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/11/08, 1/20/09, 2/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-13 have been cancelled.

Claims 14-59 have been added.

2. Claims 32-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 16, 2008.

3. Claims 14-31 are under examination.

4. The following office action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on June 11, 2008, January 20, 2009, and February 24, 2009 were filed after the mailing date of the first action on the merits on June 12, 2008. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

Objections Withdrawn

6. The objections to the specification are withdrawn in view of applicant's amendment to the specification.

Rejections Withdrawn

7. The rejection of claim 3 under 35 U.S.C. 112, first paragraph, as lacking enablement is withdrawn in view of applicant's cancellation of the claim.

8. The rejection of claims 1, 3, and 7-11 under 35 U.S.C. 102(b) as being anticipated by Leung, et al. is withdrawn in view of applicant's cancellation of the claims.

9. The rejection of claims 1, 3, and 7-11 under 35 U.S.C. 102(b) as being anticipated by Fitzgerald, et al. is withdrawn in view of applicant's cancellation of the claims.

10. The rejection of claims 1-3 and 7-13 under 35 U.S.C. 103(a) as being obvious over Leung, et al. in view of Hudson and Kortt is withdrawn in view of applicant's cancellation of the Claims.

NEW GROUNDS of Rejection

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 17, 18, 20, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a diabody sequence having one or more amino acids substituted, inserted and/or deleted. The specification discloses a diabody consisting of SEQ ID Nos. 1 and 3 that binds to CD22. The specification does not disclose substitutions, insertions and/or deletions in SEQ ID Nos. 1 or 3. The specification does not provide sufficient written description as to the structural features of the claimed genus of diabodies having one or more amino acids substituted, inserted and/or deleted.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]. " See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus

after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.).

It has been well known that minor structural differences even among structurally related compounds can result in substantially different biology, expression and activities. Based on the instant disclosure one of skill in the art would not know which residues are essential, which residues are non-essential and what particular sequence lengths identify essential sequences for identifying a diabody encompassed by the claimed specificity. For example, there is insufficient guidance based on the reliance of disclosure of SEQ ID Nos. 1 and 3 to direct a person of skill in the art to select or to predict particular sequences as essential for constructing a diabody that binds CD22. Mere idea of function is insufficient for written description; isolation and characterization at a minimum are required.

Skolnick et al (Trends in Biotechnology, 2000. Vol. 18, pages 34-39, as cited on the PTO-892 mailed June 12, 2008) teach that the skilled artisan is well aware that

assigning functional activities for any particular protein or protein family based on sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to function of the structurally related protein (see in particular "Abstract" and Box 2).

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology, 1990. Vol. 111, pages 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology, 1988. Vol 8, pages 1247-1252).

For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species cannot be achieved by disclosing only one species within the genus. In the instant case, applicant has not even disclosed a single species encompassed by the highly variant genus nor is there disclosure of the common attributes or features (i.e., structural domains) that are essential for activity or those which are non-essential. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would

provide individual support for each species that the genus embraces. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v.Baird*, 30 USPQ2d 1481, 1483. In *Fiddles v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only the diabody consisting of SEQ ID Nos. 1 and 3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

14. Claims 14 and 23-27 are rejected under 35 U.S.C. 102(a) as being anticipated by Tedder (US PG PUB 2003/0202975, published October 30, 2003).

The claims recite a diabody that recognizes CD22, wherein the diabody induces apoptosis of a tumor cell expressing CD22, wherein the diabody induces lymphoma or leukemia cell apoptosis, wherein the diabody is a dimer of two scFV, held together by non-covalent bonds, wherein the diabody is a single chain diabody, wherein the diabody is human or humanized.

Tedder teaches a diabody that binds CD22 with pro-apoptotic properties for the treatment of leukemia (paragraph 4). Tedder teaches the diabody may be chimeric, humanized, primatized or human (paragraphs 26-27). Tedder teaches diabodies comprise a heavy chain variable domain connected to a light chain variable domain with a short linker (thus a single chain, see paragraphs 60-61). Since the claims do not define the specific sequence of the diabody and Tedder teaches a diabody that binds to CD22 all the limitations of the claims have been met.

15. Claims 14 and 23-27 are rejected under 35 U.S.C. 102(a) as being anticipated by Tuscano, et al. (US PG PUB 2004/0001828, published January 1, 2004).

The claims have been described supra.

Tuscano, et al. teach a diabody that binds CD22 with pro-apoptotic properties for the treatment of leukemia (paragraph 4). Tuscano, et al. teach the diabody may be chimeric, humanized, primatized or human (paragraphs 23-24). Tuscano, et al. teach diabodies comprise a heavy chain variable domain connected to a light chain variable domain with a short linker (thus a single chain, see paragraphs 56-57). Since the claims do not define the specific sequence of the diabody and Tuscano, et al. teach a diabody that binds to CD22 all the limitations of the claims have been met.

16. Claims 14 and 23-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Tedder (US PG PUB 2003/0202975, priority to February 21, 2002).

The claims have been described supra.

Tedder teaches a diabody that binds CD22 with pro-apoptotic properties for the treatment of leukemia (paragraph 4). Tedder teaches the diabody may be chimeric, humanized, primatized or human (paragraphs 26-27). Tedder teaches diabodies comprise a heavy chain variable domain connected to a light chain variable domain with a short linker (thus a single chain, see paragraphs 60-61). Since the claims do not define the specific sequence of the diabody and Tedder teaches a diabody that binds to CD22 all the limitations of the claims have been met.

17. Claims 14 and 23-27 are rejected under 35 U.S.C. 102(e) as being anticipated by Tuscano, et al. (US PG PUB 2004/0001828, priority to February 21, 2002).

The claims have been described supra.

Tuscano, et al. teach a diabody that binds CD22 with pro-apoptotic properties for the treatment of leukemia (paragraph 4). Tuscano, et al. teach the diabody may be chimeric, humanized, primatized or human (paragraphs 23-24). Tuscano, et al. teach diabodies comprise a heavy chain variable domain connected to a light chain variable domain with a short linker (thus a single chain, see paragraphs 56-57). Since the claims do not define the specific sequence of the diabody and Tuscano, et al. teach a diabody that binds to CD22 all the limitations of the claims have been met.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
March 11, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643